Compositions and Methods for Treatment of Glucose Metabolism Disorders

Related Application Information

This Application is a Continuation-in-Part of Application Ser. No. 09/156,102, now U.S. Patent 6,376,548, filed September 17, 1998, and this Application claims the benefit of priority under 35 U.S.C. section 119(e) to Provisional Application 60/126,489, filed March 26, 1999, both of which Applications are hereby incorporated by reference in their entirety.

Background of the Invention

Diabetes adversely affects the way the body uses sugars and starches which, during digestion, are converted into glucose. Diabetes mellitus is generally caused in almost all instances by diminished rates of insulin secretion (absolute or relative) by the beta cells of the islets of Langerhans in the pancreas or by reduced insulin sensitivity. Insulin, a hormone produced by the pancreas, makes the glucose available to the body's cells for energy. In muscle, adipose (fat), and connective tissues, insulin facilitates the entry of glucose into the cells by an action on the cell membranes. The ingested glucose is normally converted in the liver to CO_2 and H_2O (50%); to glycogen (5%); and to fat (30-40%), the latter being stored in fat depots. Fatty acids from the adipose tissues are circulated, returned to the liver for re-synthesis of triacylglycerol and metabolized to ketone bodies for utilization by the tissues. The fatty acids are also metabolized by other organs.

The net effect of insulin is to promote the storage and use of carbohydrates, protein and fat. Insulin deficiency is a common and serious pathologic condition. Diabetes is commonly divided into two types: Type 1 diabetes (juvenile-onset, insulin-dependent diabetes mellitus [IDDM]) that usually, but not always, begins in early life, and Type 2 diabetes (maturity-onset diabetes, non-insulin dependent diabetes mellitus [NIDDM]) that usually, but not always, begins in later life. In Type 1 diabetes, the pancreas produces little or no insulin, and insulin must be injected daily. In Type 2 diabetes, the pancreas retains the ability to produce insulin and in fact may produce higher than normal amounts of insulin, but the amount of insulin is relatively insufficient, or less than fully effective, because of cellular resistance to insulin. Type 2 diabetes may present as non-obese